

What is claimed is:

1. A human erythropoietin polypeptide variant comprising, a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a 5 functional fragment thereof.
2. The human erythropoietin polypeptide variant of claim 1, further comprising an amino acid difference located outside an Epo-modification region.
3. The human erythropoietin polypeptide variant of claim 2, 10 wherein said amino acid difference is located at amino acid position 146.
4. The human erythropoietin polypeptide variant of claim 1, further comprising an amino acid difference in a third Epo-modification region.
5. The human erythropoietin polypeptide variant of claim 4, further comprising an amino acid difference located outside an Epo-modification 15 region.
6. The human erythropoietin polypeptide variant of claim 5, wherein said amino acid difference is located at amino acid position 146.
7. The human erythropoietin polypeptide variant of claim 1, wherein said enhanced erythropoietin activity comprises increased erythroid 20 precursor proliferation.
8. The human erythropoietin polypeptide variant of claim 1, wherein said enhanced erythropoietin activity comprises increased erythroid precursor differentiation.

9. The human erythropoietin polypeptide variant of claim 1, wherein said enhanced erythropoietin activity comprises a faster time to reach a maximal level of an erythropoietin activity.

10. The human erythropoietin polypeptide variant of claim 9, 5 wherein said enhanced erythropoietin activity comprises a faster time to reach a maximal level of erythroid precursor proliferation.

11. A human erythropoietin polypeptide variant comprising, a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a 10 functional fragment thereof.

12. The human erythropoietin polypeptide variant of claim 11, further comprising an amino acid difference located outside an Epo-modification region.

13. The human erythropoietin polypeptide variant of claim 12, 15 wherein said amino acid difference is located at position 146.

14. The human erythropoietin polypeptide variant of claim 11, further comprising an amino acid difference in a third Epo-modification region.

15. The human erythropoietin polypeptide variant of claim 14, 20 further comprising an amino acid difference located outside an Epo-modification region.

16. The human erythropoietin polypeptide variant of claim 15, wherein said amino acid difference is located at position 146.

17. The human erythropoietin polypeptide variant of claim 11, 25 wherein said moderated erythropoietin activity comprises decreased erythroid precursor proliferation.

18. The human erythropoietin polypeptide variant of claim 11, wherein said moderated erythropoietin activity comprises decreased erythroid precursor differentiation.

19. The human erythropoietin polypeptide variant of claim 11, 5 wherein said moderated erythropoietin activity comprises a slower time to reach a maximal level of an erythropoietin activity.

20. The human erythropoietin polypeptide variant of claim 19, wherein said moderated erythropoietin activity comprises a slower time to reach a maximal level of erythroid precursor proliferation.

10 21. A human erythropoietin polypeptide variant, having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 15 212, 218, 220, 222, 224, or a functional fragment thereof.

22. An isolated nucleic acid molecule, comprising a nucleic acid sequence encoding a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 20 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, or a functional fragment thereof.

23. A vector comprising the isolated nucleic acid molecule of claim 22.

25 24. A host cell comprising the vector of claim 23.

25. A method of producing a human erythropoietin polypeptide variant, comprising growing the host cell of claim 24 under conditions sufficient for expression of said erythropoietin polypeptide variant.

26. The method of claim 25, further comprising isolating said 5 erythropoietin polypeptide variant from the host cell or host cell medium.

27. An antibody or functional binding fragment thereof comprising, a region that specifically binds to a human erythropoietin polypeptide variant comprising an amino acid sequence as shown in SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60; 62, 66, 68, 70, 72, 74, 76, 82, 10 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224.

28. A composition, comprising a human erythropoietin polypeptide variant comprising an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 15 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, and a pharmaceutically acceptable medium.

20 29. A method of increasing erythrocytes in an individual, comprising administering to said individual an effective amount of a composition of claim 28.

30. The method of claim 29, wherein said individual is anemic.

25 31. The method of claim 29, wherein said individual has chronic renal failure.

32. The method of claim 29, wherein said individual has cancer.

33. A method for reducing an effect of a neurological condition in an individual, comprising administering to said individual an effective amount of a composition of claim 29.

34. A method of measuring erythroid precursor proliferation activity of an erythropoietin polypeptide over time, comprising:

(a) contacting an erythroid precursor cell line with said erythropoietin polypeptide and a non-toxic proliferation-sensitive dye under conditions sufficient for cell viability, and

(b) measuring a signal of said dye at various times after 10 said contacting,

wherein changes in said signal of the dye correlate with erythroid precursor proliferation activity.

35. The method of claim 34, wherein said erythropoietin polypeptide further comprises a human erythropoietin polypeptide variant.